



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2014-D-0090]

Retrospective Review of Premarket Approval Application Devices; Striking the Balance  
Between Premarket and Postmarket Data Collection

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice; request for comments.

SUMMARY: The Food and Drug Administration (FDA) is announcing the progress of the Center for Devices and Radiological Health (CDRH) on its 2014-2015 Strategic Priority “Strike the Right Balance Between Premarket and Postmarket Data Collection.” To achieve this priority, CDRH established a goal to assure the appropriate balance between premarket and postmarket data collection to facilitate and expedite the development and review of medical devices, in particular high-risk devices of public health importance, and established a target date of December 31, 2014, by which to review 50 percent of product codes subject to a premarket approval application (PMA) that are legally marketed to determine whether or not, based on our current understanding of the technology, to rely on postmarket controls to reduce premarket data collection, to shift some premarket data collection to the postmarket setting, or to pursue down-classification. CDRH has taken such actions periodically in the past consistent with the medical device statutory framework but typically has done so on an ad hoc basis. CDRH also will require more data or up-classify a device, if warranted, based on the current state of the science;

however, up-classification is not warranted for the devices subject to this retrospective review because they are already in the highest risk classification. In this document, CDRH is providing its current thinking on reviewed product types to solicit comments on the product codes that have been identified as candidates for reclassification, for reliance on postmarket controls to reduce premarket data collection, or a shift in premarket data collection to the postmarket setting.

DATES: Submit either electronic or written comments by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER]. See section IV for more information on how to submit comments to this document and properly identify the device(s) the comment concerns.

ADDRESSES: Submit electronic comments to <http://www.regulations.gov>. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Identify comments with the docket number found in brackets in the heading of this document and with the product code(s) for the device(s) the comment concerns.

FOR FURTHER INFORMATION CONTACT: Nancy Braier, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, rm. 5454, Silver Spring, MD 20993-0002, 301-796-5676.

SUPPLEMENTARY INFORMATION:

## I. Background

One of three Strategic Priorities for 2014-2015 in CDRH is to “Strike the Right Balance Between Premarket and Postmarket Data Collection” (Ref. 1).<sup>1</sup> CDRH’s vision is for patients in

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<sup>1</sup> CDRH’s 2014-2015 Strategic Priorities include “Strengthen the Clinical Trial Enterprise” and “Provide Excellent Customer Service,” in addition to “Strike the Right Balance Between Premarket and Postmarket Data Collection” (Ref. 1).

the United States to have first in the world access to high-quality, safe, and effective medical devices of public health importance. A key determinant of early U.S. patient access to high-quality, safe, and effective devices is the extent of premarket data that device developers provide to FDA. Once a device developer decides to seek U.S. marketing approval or clearance, the extent of data that is collected premarket has an impact upon the length of time needed to complete a premarket submission--the more data to be collected premarket, the longer it may take to acquire the data and make the submission. Consequently, such data collection issues affect when U.S. patients have access to a medical device. On the other hand, it is also important that there is sufficient data to demonstrate a reasonable assurance of safety and effectiveness before a device subject to a premarket approval application (PMA) is approved for marketing in the United States. For this reason, it is important that CDRH strike the right balance between premarket and postmarket data collection. If CDRH can shift--when appropriate--some premarket data collection to the postmarket setting, CDRH could improve patient access to high-quality, safe, and effective medical devices of public health importance. However, patient safety could be undermined if CDRH shifted some data collection from the premarket to the postmarket setting without adequate assurances that necessary and timely data collection will occur. For this reason, CDRH strives to balance the premarket data and postmarket collection, in accordance with section 513(a)(3)(C) (21 U.S.C. 360c(a)(3)(C)) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act), which directs CDRH to consider whether the extent of data that otherwise would be required for approval of a PMA with respect to effectiveness can be reduced through reliance on postmarket controls.

In order to achieve the proper balance between premarket and postmarket data collection, CDRH resolved in its Strategic Priorities for 2014-2015 to take several actions. CDRH

committed to developing and seeking public comment on a framework for when it would be appropriate to shift premarket data collection to the postmarket setting. Pursuant to this commitment, CDRH and the Center for Biologics Evaluation and Research (CBER) issued the draft guidance, “Balancing Premarket and Postmarket Data Collection for Devices Subject to Premarket Approval” on April 23, 2014 (78 FR 22690). This draft guidance proposed an FDA policy of balancing premarket and postmarket data collection during the Agency’s review of PMAs. This guidance outlined how FDA would consider the role of postmarket information in determining the appropriate type and amount of data that should be collected in the premarket setting to support premarket approval, while still meeting the statutory standard of a reasonable assurance of safety and effectiveness. Comments on this draft guidance were collected through July 22, 2014, and the guidance was finalized on April 13, 2015 (Ref. 2). Furthermore, under existing authorities, CDRH and CBER issued a draft guidance document on April 23, 2014 (78 FR 22691), entitled “Expedited Access for Premarket Approval Medical Devices Intended for Unmet Medical Need for Life Threatening or Irreversibly Debilitating Diseases or Conditions.” This draft guidance described FDA’s proposal for a new, voluntary expedited access PMA program for certain medical devices to facilitate patient access to these devices by expediting the development, assessment, and review of certain devices that demonstrate the potential to address unmet medical needs for life threatening or irreversibly debilitating diseases or conditions. To expedite access for devices addressing unmet needs, this pathway to market would shift appropriate premarket data collection to the postmarket setting while maintaining the statutory standard of a reasonable assurance of safety and effectiveness. Comments on this draft guidance were collected through July 22, 2014, and the guidance was finalized and issued on April 13, 2015 (Ref. 3). In addition, CDRH is currently developing a mechanism to prospectively assure

the appropriate balance of premarket and postmarket data collection for new devices subject to a PMA.

Another action in pursuit of the goal to strike the right balance between premarket and postmarket data collection is to commit to conducting a retrospective review of all PMA product codes (procodes) with active PMAs approved prior to 2010 to determine whether data typically collected premarket could be shifted to the postmarket setting, premarket data collection could be reduced through reliance on postmarket controls, or devices could be reclassified (down-classified) in light of our current understanding of the technology (Ref. 1). In general, some premarket data collections for class III devices that are currently marketed may be reduced through reliance on postmarket controls, or shifted to the postmarket setting if warranted based on CDRH's review experience as well as the postmarket performance and the current body of evidence regarding the benefit-risk profile of these devices. CDRH currently receives PMA submissions on the majority of these class III devices, and a change in premarket data collection is expected to expedite the approval of future PMA submissions. CDRH has periodically taken such actions consistent with the medical device statutory framework but has typically done so on an ad hoc basis. On the other hand, CDRH routinely requires more data when warranted based on our current understanding of that type of technology or based on issues raised by the data submitted by a sponsor for their device. CDRH will also up-classify a device, if warranted, based on the current state of the science. For example, in May 2014, CDRH proposed to up-classify surgical mesh when intended for use for pelvic organ prolapse (79 FR 24634), and in June 2014, CDRH issued a final order up-classifying sunlamps and sunlamp products (tanning beds/booths) (79 FR 31205). However, up-classification is not warranted for the devices subject to this retrospective review, because they are already in the highest risk classification.

During this retrospective review, the devices are analyzed according to procode. CDRH targeted the date of December 31, 2014, to review 50 percent of procodes subject to a PMA that are legally marketed to determine whether or not to change premarket data collection by shifting to the postmarket setting, reducing premarket data collection through reliance on postmarket controls, or pursuing reclassification (Ref. 1). This target extends to have 75 percent completed by June 30, 2015, and 100 percent completed by December 31, 2015.

The purpose of this Federal Register notice is to solicit comments on the procodes that have been identified as candidates for reclassification, a reduction in premarket data collection through reliance on postmarket controls, or a shift in premarket data collection to postmarket for those procodes reviewed through December 31, 2014. Efforts to reclassify and to communicate changes to data collections with stakeholders will be prioritized based on both the public health impact and Center resources.

## II. Progress toward Goal Targets

Retrospective analysis of the class III medical device procodes is intended to determine if current classifications and data collections remain appropriate for determining a reasonable assurance of safety and effectiveness. As our understanding of the technology associated with individual medical devices has increased and we have a better understanding of the risks associated with the technology of each device, the type and amount of data that is needed to demonstrate a reasonable assurance of safety and effectiveness evolve. This evolution to require the least burdensome amount of data to evaluate device effectiveness follows the least burdensome provisions of the FD&C Act (section 513(a)(3)(D)(ii)). Under section 513 of the FD&C Act, a device is a class III device and requires premarket approval if general controls and special controls are insufficient to provide reasonable assurance of the safety and effectiveness of

the device, and if the device is to be used for supporting or sustaining human life or of substantial importance in preventing impairment of human health or if the device presents a potential unreasonable risk of illness or injury. In order to reclassify a class III device into class II, the device must meet the statutory criteria for class II: A device which cannot be classified as a class I device, because general controls are insufficient to provide reasonable assurance of the safety and effectiveness of the device, and for which there is sufficient information to establish special controls to provide such assurance. As new information becomes available over time, the accumulated information available for a device may be sufficient to establish special controls to provide a reasonable assurance of safety and effectiveness; therefore, the classification of the device may be changed either up or down.

In February 2014, CDRH began its retrospective review with procodes associated with active PMAs approved prior to 2010. PMA procodes created since 2010 were not included in this retrospective review because these recently created procodes do not yet have sufficient new information for a change in FDA's current understanding of the device's postmarket performance profile. As of December 31, 2014, CDRH reviewed 69 percent of the procodes included in this retrospective review, exceeding its 50 percent review target.

The results of this analysis include recommendations for procodes that are candidates for reclassification, a reduction in premarket data collection through reliance on postmarket controls, or a shift in premarket data collection to postmarket collection. These results are published online at

<http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHVisionandMission/default.htm>. As discussed in further detail, for the purposes of this retrospective review, we evaluated each procode on a balance of factors to determine the current

benefit-risk profile and if our review indicates special controls could be established to provide a reasonable assurance of safety and effectiveness. If so, the corresponding procode was listed in the category “Candidates for Reclassification to Class II” (Table 1). If it was determined that special controls would not be sufficient to provide reasonable assurance of the safety and effectiveness of the device, then the procode was evaluated to determine if some premarket data collection for PMA submission could be shifted to postmarket collection, or if premarket data collection could be reduced through reliance on postmarket controls. If it was determined that a change of data collection could continue to provide reasonable assurance of the safety and effectiveness of the device, then the procode was listed in the category “Candidates for reduction of data collection through reliance on postmarket controls or shift of data collection from premarket to postmarket” (Table 2). This category includes procodes for which premarket data collection could be shifted to postmarket data collection, premarket data collection could be decreased through reliance on postmarket controls, or postmarket data could no longer be needed. Finally, Table 3 includes procodes for which a reduction in data collection through reliance on postmarket controls or shift in data collection from premarket to postmarket and/or reclassification occurred in 2014, during FDA’s retrospective review of PMAs.

In this retrospective review, postmarket performance data, technology and performance considerations, and other relevant considerations were evaluated for each procode. These factors were used to evaluate the current benefit-risk profile to determine if the devices are good candidates for a reduction in premarket data collection through reliance on postmarket controls, a shift of premarket data collection to postmarket, or reclassification. Postmarket performance data (including recent PMA Annual Reports, literature reviews, total product lifecycle reports, medical device reporting analysis, market penetration, and recall analysis) were investigated for

any performance concerns or problems that outpace any increases in device use or acceptance. In evaluating the technology and performance considerations for the procodes, performance concerns or problems that were uncovered in the review of postmarket data were considered unfavorable factors for a change in data collection or reclassification. Favorable factors to indicate a device is a good candidate for a change in data collection or reclassification included if risks are now well understood and determined to be moderate to low, technology uncertainties have been alleviated, performance standards or non-clinical tests have been developed that could be surrogates for some clinical testing, the need for a controlled study could be eliminated due to defined objective performance criteria, the device has been shown to have good short-term performance, or concerns are limited to long-term performance or rare adverse events.

Finally, several relevant considerations were evaluated for each procode. Unfavorable factors for devices to be considered candidates for a change in data collection or reclassification included if there have been significant changes implemented to address safety or effectiveness since the devices have been on the market or if the review of annual reports and manufacturing changes has been important to maintain safety of the devices. Furthermore, if there were a limited number of approvals or limited clinical use of the devices, this was considered an additional unfavorable factor for the devices to be considered candidates for a change in data collection or reclassification, due to inadequate data needed to conduct this scientific assessment.

After completion of this retrospective review, FDA will prioritize the procodes identified as candidates for reclassification (Table 1) according to public health impact and Center resources, in order to determine the top priority procodes for which reclassification would have the greatest impact. The procodes identified as top priority candidates for reclassification will proceed through the reclassification procedures according to 21 CFR part 860. FDA will also

prioritize the procodes identified as candidates for a change in data collection (Table 2) according to public health impact and Center resources, in order to determine which reductions of or shifts to data collection would have the greatest impact. The FDA encourages firms to submit a presubmission to get feedback on their data collection plan or contact the appropriate review branch for additional information if they are in the process of developing a device in one of these categories.

### III. Paperwork Reduction Act of 1995

This document refers to previously approved collections of information found in FDA regulations. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). The collections of information in 21 CFR part 814 have been approved under OMB control number 0910-0231.

### IV. Comments

Interested persons may submit either electronic comments regarding this document to <http://www.regulations.gov> or written comments to the Division of Dockets Management (see ADDRESSES). It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document and the product code(s) for the device(s) the comment concerns. Citizen petitions and petitions for reclassification should not be submitted to the docket. Rather, for instructions on how to appropriately submit citizen petitions and petitions for reclassification, please see 21 CFR 10.30 and 860.123, respectively. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at <http://www.regulations.gov>.

## V. References

The following references have been placed on display in the Division of Dockets Management (see ADDRESSES) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. FDA, “CDRH 2014-2015 Strategic Priorities,” 2014, available at <http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHVisionandMission/UCM384576.pdf>.
2. “Guidance for Industry and FDA Staff: Balancing Premarket and Postmarket Data Collection for Devices Subject to Premarket Approval,” April 2015, available at <http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-meddev-gen/documents/document/ucm393994.pdf>.
3. “Guidance for Industry and FDA Staff: Expedited Access for Premarket Approval and De Novo Medical Devices Intended for Unmet Medical Need for Life Threatening or Irreversibly Debilitating Diseases or Conditions,” April 2015, available at <http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-meddev-gen/documents/document/ucm393978.pdf>.

Dated: April 22, 2015.

Peter Lurie,

Associate Commissioner for Public Health Strategy and Analysis.

[FR Doc. 2015-09884 Filed: 4/28/2015 08:45 am; Publication Date: 4/29/2015]